Remarks

Claims 1-6 are pending. Claims 1-6 have been amended to recite "peptide fragment". Support for this amendment can be found, for example, on page 11, lines 9-11, and page 12, lines 20-24 of the specification.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The claims are directed to osteopontin peptide fragments and ostepontin derived peptide fragements comprising SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID NO:15. Definitions for these peptides are provided at page 11, lines 9-11, an dpage 12, lines 20-24. The peptide fragments increase cell attachment to a biomaterial and cell spread through binding to integrins on the cell surface.

One of ordinary skill in the art would be able to readily ascertain the functional binding activity of the peptides to integrins found on the surface of any cell type based upon the disclosure and the assays taught in the present specification. For example, Example 12 of the originally filed application illustrates the relative ease in which one of ordinary skill in the art may identify peptides exhibiting the claimed activities. Plates are coated with any of osteopontin, SEQ ID NO:15, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or SEQ ID NO:14. The plates are then cultured with osteoprogenitor cells and the cells undergo a transformation from a neutral (uncoated condition) to a proactive condition in

which the number of attached cells, as well as the percent spread, significantly increases (see Table 8).

The guidance in the specification and ease in carrying out the assays, as shown in the examples, clearly enables one to culture plates with other types of cells expressing different types of receptor/integrin molecules, and assay for cell attachment and/or cell spread. Integrins are the principal receptors on animal cells for binding most extracellular matrix proteins, including collagen, fibronectin, and laminin, thus, they are found on the surface of numerous cell types (see, for example, *Molecular Biology of the Cell.* IV. Cells in Their Social Context. 19. Cell Junctions, Cell Adhesion, and the Extracellular Matrix, Garland Publishing (1994)). Although the specification uses osteoprogenitor cells as an example, one of ordinary skill in the art would know that the osteopontin-derived peptides of this invention would be able to interact with integrins found on diverse cell types, such as those recited in claim 6.

Table 8 also illustrates 1) antibodies to integrins (i.e., $\alpha_v\beta_3$) inhibit the percentage of attached cells and cell spread induced by the peptides (i.e., SEQ ID NO: 15), indicating that the peptides interact with integrins; and 2) each of SEQ ID NO:15, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or SEQ ID NO:14 binds to osteoprogenitor cells and significantly increase cellular attachment over the control.

The Examiner suggests that the data demonstrating the binding of SEQ ID NO: 15 to $\alpha_v\beta_3$ in Table 8 cannot be extrapolated to SEQ ID NO: 11 (or any other osteopontin derived peptide) binding any integrin on any cell type, because SEQ ID NO: 15 was still able to cause human osteoprogenitor cells to attach and spread in the presence of antibodies against CD44 and $\alpha\beta_1$. However, just because the antibodies against CD44 and $\alpha\beta_1$ failed to inhibit cell attachment

and spreading does not mean that the peptide does not bind to these particular receptors. It most likely means that peptide-induced cell migration and cell spread in osteoprogenitor cells may preferentially occur through a specific integrin or integrins (i.e., $\alpha_v\beta_3$). However, other integrins may modulate this activity in other cell types. See, for example, Tuck et al. J. Cell Biochem 78(3): 465-475 (2000) (attached), which describes the osteopontin-induced migration of several mammary epithelial cell lines. The study demonstrates that the spread of one of the cell lines was $\alpha_v\beta_5$ and β_1-integrin dependent, but $\alpha_v\beta_3$-independent, while that of another cell line was $\alpha_v\beta_3$-dependent. Therefore, even though it is well known that osteopontin binds to $\alpha_v\beta_3$ (Hu et al. J. Biol. Chem. 270 (44): 26232-26238 (1995) (attached)), antibodies to this integrin would not block the osteopontin-induced migration of the first cell line. Finally, one of ordinary skill in the art would expect that other osteopontin-derived peptides besides SEQ ID NO: 15 would bind to integrins due to the sequence homology between the peptides and the presence of the required motifs recognized by integrins.

Applying the *Wands* factors, especially the state of the prior art and the relative skill of those in the art, to the claimed invention, shows no basis for finding that undue experimentation would be required. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.1988).

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection as it is applied to the claims as amended.

The claims now recite "fragment" which is a defined term in the specification, as discussed above. See also page 7, line 23 to page 8, line 26, stating that the invention features active osteopontin **fragments** or osteopontin-derived **fragments**, which have cell attachment or chemotactic activity. The term "fragment", which, according to the dictionary, means "an incomplete portion", implies that these peptides are not **full-length** osteopontin, but only a part of the full sequence. See attached definition of fragment.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The addition of the term "peptide fragment" should now clarify the metes and bounds of the claim. Applicants are claiming an osteopontin-derived peptide fragment comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 7-15, wherein the peptide fragment is not full-length osteopontin.

Objections

The amendment filed November 21, 2003 has been objected to under 35 U.S.C. 132. The Examiner alleges that it introduces new matter not supported by the original disclosure (claim 1). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. The objected to language has been deleted.

Allowance of claims 1-6 is respectfully solicited.

Respectfully submitted,

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Date: May 11, 2004

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein is being facsimile transmitted on the date shown below to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Hershey Miller

Date: May 11, 2004